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W. W. KEEN, M. D., LL. D.,

Professor of the Principles of Surgery and of Clinical Surgery
in the Jefferson Medical College (Philadelphia, U. S. A.)

AND

W. G. SPILLER, M. D.,

Professor of Diseases of the Nervous System in the Philadelphia Polyclinic (U. S. A.)

ON RESECTION OF THE GASSERIAN GANGLION

WITH A PATHOLOGICAL REPORT ON SEVEN GANGLIA

REMOVED BY PROFESSOR KEEN.

ON RESECTION OF THE GASSERIAN GANGLION

Up to the present time I have done eleven operations for the removal of the Gasserian ganglion. The first of these cases was reported in the *Transactions of the Philadelphia County Medical Society* for 1894 and in the *Medical and Surgical Reporter* for March 1894 in conjunction with Dr. John K. Mitchell. It was the fourteenth operation done on the patient. From the date of that operation, October 18th, 1893, the patient has been well, though his condition of mental anxiety lest the pain should return and his mental instability as a result of his long continued use of opium are very marked, yet practically he is well of his neuralgia. He still has pain, but not the old tic.

In the *American Journal of the Medical Sciences* for January 1896, I reported five additional cases. The later history of these cases is as follows :

CASE II.

The operation was done June 18th, 1894. No ganglionic cells or nerve fibres were found in the tissue supposed to have been removed from the site of the ganglion. The pain returned in six months, though not so badly as before. It still continues. (September 1897).

CASE III.

Died in a week from septic infection

CASE IV.

The operation was done May 23rd, 1895 and at present, September 29th, 1897, she is entirely well.

Of cases V and VI, I append a brief summary, since the examination of the specimens from these two cases is an important part of the pathological report which follows.

Of the remaining five cases (VII to XI inclusive), which have never been reported, I give only a brief résumé of each sufficient to compare with the pathological report. I shall publish them more fully hereafter.

In conjunction with my own remarks on the removal of the ganglion and as a very important addition to our knowledge of the pathology of tic douloureux, I have been so fortunate as to secure the cooperation of my friend, Prof. William G. Spiller, who has examined with great care these seven specimens which I had removed, and which were as yet unexamined. In all of these ganglionic tissue was found. These specimens cover the cases V and VI of my second paper, and all the five additional cases (VII-XI inclusive) here briefly reported. I consider myself most fortunate in being able to enlist the services of so accomplished a neuropathologist as Prof. Spiller, and the value of his contribution will be seen not only in the text, but in the beautiful illustrations, for which we are indebted to the skill of Miss A. G. Newbold.

It will be observed that of the eleven, ten were secondary operations, multiple peripheral operations have been done in all the cases before the ganglion itself was attacked, with the exception of one case (Case VIII). In this case,

all of the branches being involved, I removed the ganglion at once. All of the operations were done by the Hartley-Krause method. Of the eleven, three died, one from direct and avoidable infection (Case III), the other two of shock.

In six cases (VI-XI) an attempt was made to remove the entire ganglion, and the photographs show that I was perfectly successful in Cases VI and XI in removing the entire ganglion with its roots, and successful in removing at least the ganglion itself in all the others. In Case VI, in which the entire ganglion, including its second and third divisions and its sensory and motor roots were removed, Prof. Spiller was able to obtain sections which showed the microscopical condition of the ganglion as well as its physical relations with its sensory root and peripheral branches all in a single slide. As the motor root joins the third branch on the distal side of the ganglion, it could not, of course, be cut in the same plane as the other portion of the ganglion. In Case VIII, we were fortunate also to have a ganglion from a case in which no peripheral operation whatever had been done.

One disadvantage Prof. Spiller has labored under is that I was not aware at the time of my operations of the technical value of Nissl's method, or I should not have preserved the specimens in Muller's fluid, which prevents their examination by that method. The cellular changes, therefore, could not be studied in all their details, but the advantages of the selected method of hardening for an examination of the alterations in the intraganglionic nerve fibres are very great.

RESUME OF CASES V TO XI.

CASE V. — *Breaking up of Gasserian ganglion after two prior operations; rupture of middle meningeal at foramen spinosum; postoperative corneal ulcer; recovery; cure for two years.*

Mrs. F., aet. 54. First consulted me July 15th, 1891. Neuralgia for twelve years in the inferior dental. In april 1878 Dr. Agnew removed a half inch of the inferior dental; relief for eighteen months. When seen in 1891,

had neuralgia in both second and third divisions. On July 17th, 1891 I removed the inferior dental and the infra-orbital nerves in the orbit.

Operation, October 6th, 1895. Posterior branch of middle meningeal divided in chiselling the bone. Anterior branch torn in its canal on turning down the flap. Both branches secured with considerable difficulty. In lifting the temporo-sphenoidal lobe the middle meningeal ruptured at the foramen spinosum; controlled by Allis' dissector and packing with gauze. The second and third divisions were then divided at their foramina and grasped with forceps, but on endeavoring to remove the ganglion by traction on the two nerves, the two branches tore off from the ganglion. The ganglion itself was then removed with a curette. The cavernous sinus was visible and avoided. The gauze was removed in three days and wound healed in a week. A corneal ulcer developed, but after a great deal of trouble, the eye was saved with good vision. Sept. 25th, 1897. Is still free from pain. Vision good. Weight has risen from 96^{lbs} to 132^{lbs}.

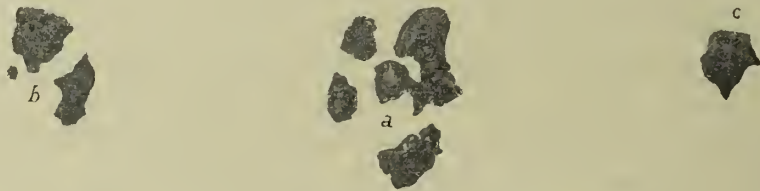


Fig. 1. — Specimen Case V: a, Gasserian ganglion; b, II division; c, III division. Natural size.

CASE VI. — *Removal of the entire ganglion intact with its second and third divisions and its sensory and motor roots back to the pons in a piece 4 cm. long after four prior operations; recovery; cure for two years; post-operative corneal ulcer.*

C. W. E., aet. 33. Neuralgia for five years. In March 1895 the right upper teeth and the alveolar process removed. Since then three other operations, including removal of the infraorbital nerve and antrum drilled.

Operation, November 22nd, 1895. Preliminary stitching of eye-lids; anterior branch of middle meningeal torn at a point where a large branch penetrated the bone. On lifting the temporo sphenoidal lobe a furious hemorrhage from the middle meningeal, ruptured one-quarter of an inch above the foramen spinosum, took place, though the lifting had been done with the greatest gentleness. Vessel ligatured; ganglion seized with a pair of hemostatic forceps before division of the second and third branches. Branches then divided and the ganglion twisted with the forceps, removing the ganglion with its second and third divisions and both roots entire. Profuse hemorrhage followed the twisting out of the ganglion; temporary packing did not arrest it, and I, therefore, packed with a strip of gauze

ten inches by one and a half (fifteen square inches), and closed the wound. The next day he complained of severe frontal headache, temperature 104° F. Though I was very loath to remove the packing, I felt forced to do so on account of the headache and the temperature. It was removed very slowly and gently, and was not followed by any hemorrhage. Within an hour the temperature had fallen to 99° F., and the headache was gone. Uneventful recovery. The stitches in the eye-lids were removed after four days; the eye-ball was normal. Within twenty-four hours corneal ulcers began, and after a great deal of trouble Dr. de Schweinitz, who had the care of his eye, was able to save it with only partial eyesight.

Oct. 5th, 1897. Muscles of mastication on right side entirely wasted and absolutely useless. Can chew meats well by using those on the left side. Right eye is still injected and cornea rather hazy. Can count fingers, but cannot read with right eye. Absolutely free from all pain ever since operation, face, including forehead, tongue, nostril, and cheek, anesthetic.

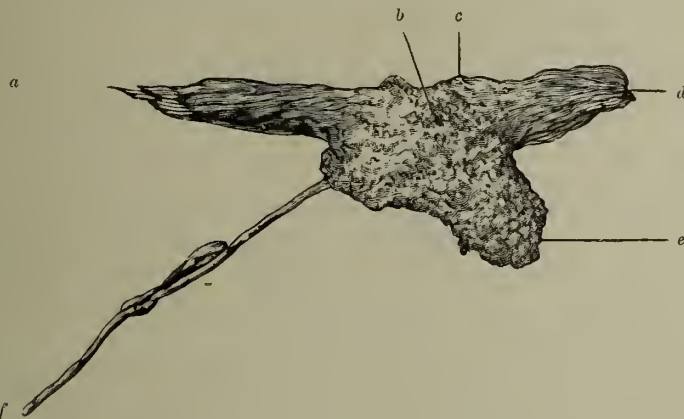


Fig 2. — Gasserian ganglion with the II and III division and the sensory and motor roots removed from Case VI. The nerve fibres are well shown. The motor root is elongated by the accidental reversal of one of its bundles. *a*, Sensory root; *b*, Gasserian ganglion; *c*, Stump of I division; *d*, II division; *e*, III division; *f*, motor root.

CASE VII. — *Removal of Gasserian ganglion with portion of its roots after two prior operations; cure for a year and nine months.*

James McM., aet. 76. In excellent health for his age. Neuralgia for twenty years in second division of right fifth nerve; no apparent cause. In 1886 Dr. Agnew resected the infra-orbital, and, in 1892, Dr. Thomas G. Morton again resected the same nerve. The pain returned soon after the second operation, and has extended to all branches of the fifth; the paroxysms being only a minute or two apart; the tongue is involved; anterior wall of antrum is gone.

Operation, December 31st, 1895. Eye-lids stitched together. Anterior branch of middle meningeal torn in turning down flap, then ligated. Dura partly ossified; ganglion seized and twisted out, the roots being imperfectly removed.

Third division tore loose and removed; no shock caused by avulsion. Went home in ten days; highest temperature 100° F.

September 25th, 1897. General health excellent; has gained twenty five pounds in weight; no return of the tic, but an obscure « creepy » feeling in his right face. Vision good.



Fig. 3. — Case VII. The larger fragment is the ganglion with part of the sensory root to the right. The thin filament to the right and below is the motor root. To the left and below is the II division. The smaller fragment is the III division broken off.

CASE VIII. — *Removal of Gasserian ganglion as a primary operation; possible tear of cavernous sinus; controlled by packing; uneventful recovery; cure for three weeks.*

Mrs. A. W. S., aet. 69. Present trouble began in 1878; all teeth removed. Pain in all three divisions.

Operation, January 24th, 1896. Eye-lids stitiched together. Anterior branch of middle meningeal in a complete canal; posterior in excessively deep groove, both torn, therefore, in turning down the flap. Both vessels ligated. Ganglion twisted out.

Second division tore loose from ganglion and, in the rush of blood following the avulsion, was lost. Hemorrhage so severe that I believed the cavernous sinus was torn; readily controlled by packing with gauze. Highest temperature third day 100°, 6 F. Gauze removed on third day, and on the same day the sutures in the eyelids removed, and the Buller shield applied.

She had no trouble with the eye. Three weeks after the operation she was free from pain. Later letters have licted no answer.

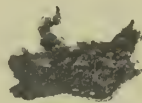


Fig. 4. — Case VIII.
Gasserian ganglion.



Fig. 5. — Case IX.
Gasserian ganglion.

CASE IX. — *Removal of Gasserian ganglion after one prior operation; wound of cerebral vessels while making osteo-plastic flap; rupture of cavernous sinus; packing with gauze; coma and hemorrhage; death in three days.*

George K., aet. 49. Pain began in 1879 in right upper canine, teeth extracted. In 1889 infra-orbital resected, giving relief for two and a half years on the cheek, but the pain in the forehead still remained. When seen, the first and second divisions were involved, but the lower jaw was not.

Operation, April 21st, 1896. In making the osteo-plastic flap, a wound of the cerebral vessels was accidentally made. When the osteo-plastic flap was turned down, a sub-dural clot amounting to one ounce of blood was removed and the dura closed. Anterior branch of middle meningeal ran in a canal, and was torn and ligated. Ganglion was then uncovered and avulsed, followed by such a copious hemorrhage that I believed I had torn the cavernous sinus. Iodoform gauze (267 square inches) packing checked the hemorrhage: reacted well, but did not become conscious. Hemiplegia was recognized. He remained unconscious and hemiplegic till his death toward the end of the third day. The gauze was removed after forty-eight hours without hemorrhage; necropsy refused.

CASE X. — *Removal of Gasserian ganglion; death in ten hours from shock.*

Mrs. M.S., aet. 63; pain for over thirty years. Second and third divisions removed some years ago; pain now exists in all three branches.

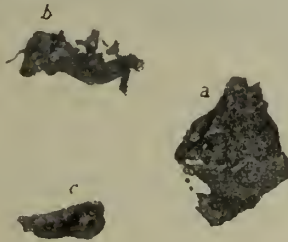


Fig. 6. — Case X. *a*, Gasserian ganglion; *b*, II division; *c*, III division.

Operation, October 31st, 1896. Anterior branch of middle meningeal in deep grooves and lacerated, but ligated. Avulsion of third and second divisions, bringing with them a considerable portion of the ganglion. Removal of ganglion; reacted well an hour after the operation, but then began to fail, and died in ten hours; necropsy refused.

CASE XI. — *Removal of Gasserian ganglion after six prior operations; cure for eight months; eye-sight lost from secondary corneal ulcer.*

Mr. F. W. P., aet. 56. Pain began in 1896 in right lower jaw; six peripheral operations had been done on the inferior dental as far back as the foramen ovale. An attempt had been made to remove the Gasserian ganglion without benefit to his pain.

Operation January 22nd, 1897. Ganglion laid bare and avulsed. Second division tore loose from the ganglion. Eye-lids stitched together at the close of the operation. Stitches removed on third day, and Buller shield applied; highest temperature 100° F. Went home thirteen days after the operation in excellent condition as to eye and pain. Protecting the eye with

a handkerchief without the shield produced friction on the cornea followed by a corneal ulcer, from which he ultimately lost his eyesight. Has been entirely free from pain up to the present time, October 1, 1897.

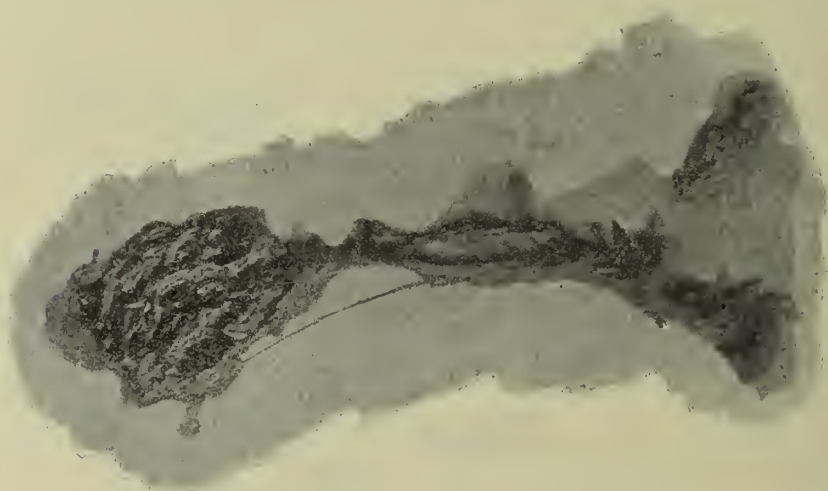


Fig. 7. — Case XI. The larger reticulated mass to the right is the Gasserian ganglion.
The detached piece is the II division.

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To sum up the results of Prof. Spiller's researches, we may say that, in a general way, the pathological changes which he has found are:

First. That the medullary substance of the nerve fibre within the ganglion and its branches is immensely swollen, atrophied, or entirely gone, depending on the intensity of the disease

Secondly. That the axis cylinders similarly are markedly degenerated or entirely destroyed.

Thirdly. That the cells of the ganglion itself, in at least one case, are so degenerated, or atrophied, that there would even be doubt whether we were dealing with ganglionic tissue were it not for the occasional nerve cells seen.

Fourthly. That the vessels are very distinctly sclerotic. In one instance the lumen is even entirely obliterated.

Fifthly. There is, in at least one case, a decided amount of increase in the connective tissue of the ganglion, which is enough to call the alteration a distinct sclerosis.

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I propose to take up four points.

First. Should the Gasserian ganglion be removed?

Secondly. The answer being in the affirmative, to what extent shall it be removed, i. e. shall we remove the entire ganglion, or only its outer two thirds, or shall we be satisfied with simply « breaking it up » by blunt instruments or a curette?

Thirdly. Should the ganglion be removed as a primary operation, or should its removal be reserved till the very last operation for tic douloureux?

Fourthly. A few points in the technique.

The removal of the Gasserian ganglion is in some respects rather peculiarly American. The first deliberate proposal to remove the Gasserian ganglion was made by Dr. J. Ewing Mears of Philadelphia (*Transactions American Surgical Association*, 1884, Vol. II, p. 469). Andrew of Chicago (*Chicago Medical Record*, 1891, Vol. I, p. 322) had been at work for eighteen months devising practically the same operation as Rose, but the latter preceded him both in publication and performance (*Lancet*, 1890, Vol. II, p. 914). Similarly Hartley of New York, and Krause of Altona, almost at the same time devised the method of operating which has been the most used, and is, on the whole, perhaps the best method.

Of the 108 cases of intracranial operations on the fifth nerve collected by Tiffany (*Transactions American Surgical Association*, 1896, Vol. XIV, p. 1; and *Annals of Surgery*, 1896, Vol. XXIV, p. 575) 79 were done by American surgeons, and 29 by European surgeons.

I. Whether we ought still to resect the ganglion depends, in my opinion, on three conditions: *a*) the mortality of the

operation; *b*) its efficiency as a means of permanent cure, and *c*) whether its disadvantages, especially the possibility of the loss of the eye on the operated side, can be avoided.

a) The mortality of the operation may be taken as that shown by Tiffany's table, in which of 108 cases, 24 died, a mortality of 22,2 %. For an operation done by modern antiseptic or aseptic methods, a mortality of over one-fifth is very large. I have no doubt it will be diminished in the future, as we learn by experience to deal with its vicissitudes and emergencies. In fact, surgically speaking, we *must* master and overcome so large a mortality. No one who has ever resected a Gasserian ganglion will speak lightly of the operation. Even now after having operated on eleven, I always approach the operation with a certain amount of hesitation. The mortality alone would cause me to answer the third question positively in favor of the resection being reserved for the last of the series of operations, instead of the first.

b) What has been the history of the cases as to cure? So far as I know, there have been only four cases in which the pain has returned; one reported by Rose, one by Dana and two by myself. But, I especially desire to call attention to the fact that my own two cases of recurrence of pain were my first two operations; that in Case I no microscopical examination of the fragments removed was made, and in Case II the examination revealed no ganglionic cells nor nerve fibres. Case I, as I now look at it, was imperfectly done, and Case II still more so. Therefore, the recurrence of pain in these two cases cannot be used as an argument against the removal of the ganglion. The facts as to recurrence of pain in these two cases have been given earlier in this paper. In addition to this, Krause has reported one case in which the sensory root was found diseased, and the pain returned on the other side of the face. We can conclude, therefore, in general, as a result

of experience in over 100 cases of intracranial operation on the fifth nerve, that, practically, the pain will not return in over 1 or 2 % in any such severity as to liken it to the original disease, and that it will not return at all in more than 4 or 5 per cent. Perhaps, if we consider the uncertainty of total excision of the ganglion in the reported cases in which pain did not return, this percentage is too high. As Prof. Spiller has shown, there are only two cases known to him in which the sensory root has been examined (although it may be that Krause examined the sensory root in some of his other cases); one of these was by Krause (*loc. cit.*, p. 113.), and one by himself. In Krause's case the root was diseased, and the pain returned upon the opposite side. In my own case (Case VI), though the lesions of the ganglion were very intense, and the disease had existed for five years, Prof. Spiller found the sensory root entirely free from any pathological changes in longitudinal as well as transverse sections. We must expect, as an inference from both the clinical history and the pathological examination of Krause's case, that the disease may not only reach, but may pass beyond the ganglion to the sensory root, and that, therefore, even the removal of the ganglion will not always absolutely prevent a return.

c) Apart from the mortality, the chief danger is the loss of vision if not of the eye-ball. This, I think, I now know how to master. I shall consider it under the question of technique. All other disadvantages, such as the possible necrosis of a piece of the bone, the sinking in of the flap, or the possible uselessness, in a certain number of cases, of the muscles of deglutition are very slight as compared with the immense relief from the horrible pain.

My conclusion, therefore, is that the removal of the Gasserian ganglion should still be done, but that we should especially strive to lessen the mortality of the operation.

II. To what extent shall the ganglion be removed?

Tiffany has expressed the opinion (1) that the motor root can be saved, and (2) that it ought to be saved. In a number of my cases, though I have made no attempt to save the motor root, the muscles of mastication, on the operated side, were not wholly paralysed. In Case VI, in which the motor root was certainly removed, the muscles of mastication, on the operated side, are atrophied and useless, but the patient can readily masticate meats, the lower jaw being easily moved by the muscles of the opposite side. I do not, however, myself believe that the motor root *can* be preserved. In the first place, I do not think that, from an operative point of view, it is possible to do so, and, secondly, the very careful dissection of the ganglion made by Jouvara (*Chipault's Traux de Neurologie chirurgicale* Vol. II, 1897, p. 205) makes me sure that this is even anatomically quite impossible. He says (pp. 209-10) « the masticatory nerve [by which I take it he means the motor root] and its branches are very adherent to the trunk of the inferior maxillary division, and are contained in the same sheath of connective tissue: the separation of these two nerves is difficult even by the most careful dissection, and to avulse the inferior maxillary without, at the same time, avulsing the masticatory nerve is veritably impossible ». Tiffany, however, is speaking of cutting the masticatory nerve *before* it becomes a part of the inferior maxillary. If this cannot be done on the dead body by the most careful dissection, how much less can it be done on the living during the exigencies of an operation.

In the microscopical examination of my case (Case VI) the motor root was found to form an intimate part of the third branch so near the ganglion that it would have been very difficult, or even impossible, to separate it from the ganglion at the time of operation. Another point is worthy of mentioning; the peripheral sensory branches must degenerate after resection of the ganglion, and it may be

that in the sclerosis which follows the destruction of the sensory fibres of the third branch, the motor fibres would be at least partly affected even if they had not been cut. The only possible absolute necessity for conserving the nerve would be the need for preserving it in case of a bilateral resection of the Gasserian ganglion. This has never yet been necessary, and will surely be extremely rare. If after destruction of the ganglion the muscles of mastication on the sound side are sufficient for the purposes of mastication, I see no reason to trouble ourselves to preserve the motor root, and thus dangerously to prolong the operation.

Secondly. A much more important question as to the extent of the removal of the ganglion is whether *a*) the entire ganglion shall be avulsed, such for example, as is seen in figure 2 from Case VI of my own series, and in several of Krause's photographs (*Neuralgie des Trigeminus*), or *b*) whether we should follow the recommendation of Tiffany that only the outer two-thirds of the ganglion, together with the second and third divisions, should be removed, and the inner third left. The only object in leaving the inner third is the conservation of vision. But, as shown below, I believe that our methods of dealing with the eye are so improved, that we can positively now remove the ganglion, and yet conserve the eye.

In addition to this, we must remember that the ganglion is not divided into thirds physically or physiologically. It is not true that the inner third of the ganglion is connected exclusively with the first division, and supplies the eye, the middle third with the second division, and the outer third with the third division; but, more or less, the cells of the ganglion in every part are connected, so far as we know, with any or all of the three divisions.

An arbitrary line, therefore, removing the outer two-thirds and leaving the inner third, will leave undoubtedly diseased ganglionic cells, if the ganglion is affected. If these

cells are diseased, any stimulus from the first division will excite sensation in them, and thus may bring about a return of the pain.

As the only objection to removing the whole ganglion — the effect upon the eye — can now, I think, be overcome, we ought, I believe, distinctly to aim at the removal of the entire ganglion.

III. Shall the ganglion be removed as a primary operation — the very first after the disease has set in —, or shall it be left till the last operation: that is to say, shall we perform as many peripheral operations as can be done first, and only remove the ganglion when we are driven to it?

I believe that this last is the proper position to take. While Prof. Spiller, from his investigations of the pathology, is not able to say positively whether the ganglion becomes diseased primarily or secondarily, yet as he points out, the clinical evidence would lead us to believe that the ganglion is the last of all to suffer. Of course, after any peripheral operation, just as after an amputation of an arm, degenerative changes will set in which will go direct to the Gasserian ganglion, and may, so far as we know, reach to the pons, or even possibly the cortex, just as after an amputation of the arm, degenerative changes can be traced into the central nervous system; yet these are very different from anything like an ascending neuritis, which would involve the ganglion in inflammatory troubles as a result of the preceding disease of the nerve branches.

The effect on the ganglion, even after eighteen years of suffering, in Case VIII, was very slight. This, so far as I know, is the only examination of a ganglion in which no peripheral operation had been done, and in which the examination is, therefore, free from any suspicions of alteration in the ganglion other than that due to a possible ascending neuritis. It must be stated, however, that the entire ganglion

could not be examined microscopically. If the ganglion is not diseased, therefore, primarily, I believe that we ought to attack the disease where we *know* it exists, namely,— in the peripheral branches. If the ganglion is primarily diseased, we cannot understand how it is that relief is afforded for one, two, or three years. The simple shock of the operation would not keep a diseased ganglion quiescent for months or years. My own conviction, based on examinations so far made, is that the disease in many cases, at least, is primarily peripheral, and that the ganglion is involved by extension upward. In those cases in which some local growth is found on the branches of the fifth nerve, the cause of the pain must, of course, be peripheral, and we have no means of detecting the presence of such a lesion previous to operation. I would, therefore, urge not only that the removal of the Gasserian ganglion should be the *last operation*, but I would specially urge that peripheral operations be done *early*. Most operations for tic douloureux are made two, three, five, ten, or even twenty years after the disease began, and after vain attempts have been made to cure by drugs. My own view decidedly is that if after the disease has positively existed for so long a period as three or four months, and if during this time, while drugs may have relieved, they have not *cured* it, I would *wait no longer, but instantly do the peripheral operation in hope of arresting the peripheral disease and preventing its upward course, which, in time, will result in its finally involving the ganglion.*

When we remember the fact that all peripheral operations are virtually without any danger to life, and that they relieve for a considerable time, and that we are in a position now to state that the mortality of Gasserian operations is over 20 per cent., and that in a small percentage of cases even the removal of the Gasserian ganglion may not surely and permanently cure, I think we are in a position to say that the removal of the ganglion should not be done till we

have exhausted our resources in peripheral operations; or till a larger surgical experience shows that the removal of the *entire* ganglion *will cure* permanently, and a better surgical technique greatly lessens the present mortality.

IV. A FEW POINTS IN TECHNIQUE. — *a) Access to the cranial cavity.* — There is no question in my mind that either



Fig. 8. — Shows the natural size of the piece of iodoform gauze (37×6 inches) packed in the cavity of the skin for three days without harm; seen edgewise.

the Hartley-Krause operation, or the operation Doyen (which I have never yet attempted), or an operation somewhat analogous to it described by Poirier in *Chipault's Travaux de Neurologie chirurgicale*, vol. II, 1897, p. 213, is the preferable one. All of these approach the ganglion from the side, and by lifting the temporo-sphenoidal lobe. By no possibility can one work with the same advantage, either as to light or facility of manipulation, by Rose's method. Whether the flap shall be raised by chisel, or drill, or saw, I think is a matter largely of preference of each individual operator.

b) Hemorrhage. — In three instances I have done the operation in two stages on account of hemorrhage, packing iodoform gauze into the skull in these cases. The amount of gauze which I have used has surprised me very much. In one case it was 37 by 6 inches, or 222 square inches of gauze (fig. 8); in a second 23 by 14 inches, or 322 square inches; in a third 267 square inches; and in a fourth a piece 16 by 6, or 96 square inches. I mention this to show what an amount of pressure the brain will stand, but I also mention it to condemn the process if it is possible to avoid it. The danger of infection is always considerable in any case in which the skull cavity has to be reopened. Moreover, I think we ought always

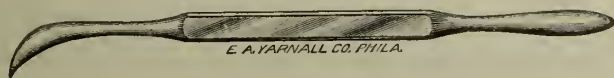


Fig. 9. — Allis's blunt dissector.

to avoid testing the power of the brain to stand pressure if we can. I join, therefore, heartily with Krause in urging that the operation shall be completed in a single sitting if possible.

Hemorrhage from the middle meningeal has almost invariably taken place in all of my operations, either by unavoidable tearing of the vessel, in turning down the flap, or, as happened three times, by the tearing of the vessel at the foramen spinosum. In the latter case, the simple use of the Allis blunt dissector (1) (Figure 9) to block up the vessel for a moment by the curved end, and later the substitution first of the left forefinger, and then of a small bit of

(1) This most useful yet simple surgical instrument is not as well known as it deserves to be, hence I figure it here. In all blunt dissections, which are so largely employed, it is simply invaluable, especially by the facility with which adhesion are torn through by its curved end.

iodoform gauze, will overcome the difficulty if the vessel cannot be ligated. On no account, in my opinion, should the external carotid be ligated as a preliminary measure. In one case in this city (Philadelphia) in which it was done, necrosis of the temporal flap took place, and the patient's death from sepsis followed as a result.

c) The removal of the ganglion itself is best done by Krause's method; namely, — uncovering the ganglion and then seizing it, and slowly twisting it out, after dividing the second and third divisions at their foramina. This method of removal should be employed instead of the uncertain method of « breaking up » the ganglion when we act blindly and unscientifically.

d) The preservation of the eye. The method which experience has taught me now definitely to adopt is as follows: — either immediately before, or at the close of the operation, I disinfect the eye, and sew the two lids together by two or three stitches, drawing together only the middle of the lids. This leaves the two ends open sufficiently, first, for washing the space between the lids and the eyeball with a warm boric acid solution to wash away any mucus, and also leaves enough space for us to observe the cornea when the patient looks strongly to one side. This occlusion of the lids should last for not less than four or five days. The stitches may then be cut, and the eye immediately covered with a Buller shield, i. e. a watch glass held in place by means of, either a circular fenestrated disk of rubber plaster, or by four separate pieces of plaster. I prefer the circular plaster.

The reason for the corneal ulceration and loss of vision, or loss of the eye, is undoubtedly, first, the drying of the cornea due to the want of appreciation of its drying, by reason of its being anaesthetic, and, therefore, to want of winking, by which the cornea is kept moist; and, secondly, as another result of the want of sensitiveness of the cornea,

either foreign bodies get into the eye, or, as in one of my cases, a bandage over the eye may rub the cornea, and thus produce ulceration and the destruction of the cornea. The use of the Buller shield is so thoroughly satisfactory, both in protecting the eye and in keeping it moist, that I think any one who has tried it will be unwilling to dispense with it afterward. Its use should be continued for from ten to thirty days after the operation.

PROFESSOR SPILLER'S PATHOLOGICAL REPORT

*From the Wistar Institute of Anatomy and Biology,
Philadelphia, U. S. A.*

Little attention has been paid to the microscopical examination of the Gasserian ganglia removed from patients suffering from tic douloureux. Indeed, with the exception of a few cases, we have had almost no information furnished us on the pathological condition of these structures in the disease. It was, therefore, with a feeling of the deepest interest that I undertook the examination of the ganglia removed by Professor Keen from seven cases of prosopalgia.

This report is based on a study of several hundred sections. The stains employed have been carmine, hematoxylin (Delafield's and Weigert's), osmic acid (methods of Azoulay and of Marchi), thionin, acid fuchsin and eosin. The method of Rosin has given most satisfactory results for a study of the nerve fibres, and in some cases, in which the material did not stain readily with carmine, Delafield's hematoxylin, with an after-stain of acid fuchsin, presented beautifully colored specimens. Unfortunately, the method of Nissl could not be employed, as all the ganglia had been placed in Müller's fluid. The method of Azoulay proved to be of great service, for in some cases in which the method of Weigert did not give thoroughly satisfactory results, the former yielded sections well stained.

CASE V.

The nerve fibres are greatly altered, in many the medullary sheaths are much swollen, and no traces of axis cylinders can be seen; in others the latter are represented by irregular and separate masses of a hyaline-like red substance, which have little resemblance to normal axis cylinders. Many nerve sheaths are entirely empty. The vessels are sclerotic, and some of the smaller ones are entirely closed. The ganglion cells are in different stages of degeneration; some are faintly stained and have very indistinct outlines, and there are numerous spaces in which the cells have entirely disappeared. Some of the nerve cells are very small, and without nuclei and nucleoli, and the connective tissue between them is increased in amount. The pericellular spaces seem to be somewhat larger than in normal ganglia, and appear as if the cells had shrunk away from their capsules. No very great difference can be noticed in the condition of the second and third branches of the nerve, for they seem to be nearly equally diseased.

CASE VI.

The ganglion removed from Case 6, presents on microscopical examination most distinct evidences of degeneration. The medullary sheaths on many of the intraganglionic fibres are greatly swollen, and the fibres have an irregular, beaded appearance in longitudinal sections. Some bundles, cut transversely, contain masses of medullary substance varying greatly in size, and of most irregular form, and without a trace of axis cylinders.

Stained by the method of Azoulay or Weigert, these masses of medullary substance stand out prominently, and it is noticed that frequently they are not continuous with

one another, but that they are connected by empty and contracted nerve sheaths. There is no great increase in the number of the nuclei of the sheaths of Schwann. Normal bundles of fibres are found lying close to fibres very greatly degenerated. It is impossible to find any greater alteration of the fibres belonging to the second than of those belonging to the third branch of the trifacial nerve.

The sensory and motor roots are normal, the nerve fibres in these roots present medullary sheaths which stain well, and have normal outlines. Longitudinal and transverse sections of the motor and sensory roots, and of the second and third branches of the nerve, have been obtained; the first branch had been broken off close to the ganglion at the time of the operation.

Transverse sections of the motor and sensory roots present the usual number of nerve fibres, each with an axis cylinder surrounded by a medullary sheath, and separated from the other by a moderate amount of connective tissue. The contrast afforded by the transverse sections of the second and third branches, with those of the sensory and motor roots, is most striking. In the second branch, especially, the irregular and large masses of medullary substance are very distinct, and in many bundles it is impossible to detect axis cylinders. Atrophied fibres seem to predominate in the transverse sections of the third branch, though in longitudinal sections, a little nearer the ganglion, the swollen medullary sheaths are as visible as in the second branch. The ganglion was cut longitudinally in such a manner that its relation to the second and third branches, and the sensory root, are shown in a single section. In some intraganglionic nerve bundles, axis cylinders may be found greatly swollen, and occurring in irregular masses of a pinkish hue when the carmine is employed as stain, but these masses are more numerous in certain bundles.

The process has evidently reached a stage in which the swollen axis cylinders have in large part been removed. The connective tissue about, and between, the bundles of nerve fibres is not very excessive, but is increased to some extent between the individual fibres.

The ganglion cells are somewhat more irregular in outline, the smaller cells are more numerous, and the pericellular spaces are larger than in normal ganglia. Many cells contain vacuoles, but the nuclei are not excentric, and the nucleolus can usually be seen. The pigmentation of the cells is not excessive, and the capsules of the cells do not appear to be much thickened, nor are their nuclei unusually numerous. The intercellular tissue is not notably increased. In some places the cells are very small and faintly stained, though a few appear unusually large and swollen, but these are comparatively rare. The most striking alteration of the cells is the atrophy with the enlargement of the pericellular spaces, of which the latter may be due to changes which have occurred after removal of the ganglion.

The small vessels in many parts of the ganglion are greatly altered, some are completely closed by the proliferation of the tissue in the walls of the vessels, while others show only a slight alteration.

CASE VII.

The ganglion cells are most irregular in shape, and appear to be somewhat more separated than normally from one another by overgrowth of the intercellular connective tissue. Some of the cells are not sharply defined from the surrounding tissue, and some do not contain distinct nuclei or nucleoli. In some places the ganglion cells have been destroyed and removed, in others the cells contain much pigment and some vacuoles. The cellular changes are greater

than in the preceding case, in which they are not especially striking. The medullary sheaths of the nerve fibres in many places are greatly swollen. Many nerve bundles contain very small nerve fibres; many are entirely deprived of nerve fibres, and contain merely connective tissue; and many contain swollen medullary sheaths without axis cylinders. The small vessels have thickened walls, and some are entirely closed by proliferated tissue.

CASE VIII.

Some of the vessels are sclerotic, but there is little change in the nerve fibres. The smaller ganglion cells are abnormally abundant. In some places the medullary sheaths are somewhat swollen.

CASE IX.

The findings in this case consist of swollen medullary sheaths, diseased axis cylinders, proliferated connective tissue in the nerve bundles, with destruction of nerve fibres, and altered ganglion cells. Only a portion of the ganglion has been obtained, but it is sufficient for the purposes of microscopical study. The cells and their capsules in certain parts, can be distinguished with difficulty from the surrounding tissue; in other parts they are much more distinct; it is frequently impossible to detect nuclei or nucleoli, and one might well doubt whether he were examining ganglionic tissue, were it not for the fact that here and there a nerve cell is detected. The intercellular tissue has replaced the ganglion cells.

The blood vessels are much altered, as may be seen in Figure *h*. In this vessel the media and intima are much thickened, and the latter has almost entirely filled the lumen of the vessel, leaving several smaller passages for the current

of blood. In the process of hardening the inner coats at one portion have contracted, and withdrawn from the outer, leaving an open space.

CASE X.

The medullary sheaths, in certain parts of the sections, are enormously swollen, and the axis cylinders have been almost entirely destroyed and removed, leaving small lumps of a pinkish hyaline substance here and there. Many nerve sheaths may be found in which the medullary substance and axis cylinders have entirely disappeared. The vessels seem to be less affected than in the other cases in which evidences of intense degeneration have been noticed. The ganglion cells have indistinct outlines, and some stain very faintly. The intercellular tissue is increased in amount, and, throughout the sections in which the ganglion cells are found, numerous granular corpuscles are noticed.

CASE XI.

The ganglion cells are vacuolated, but do not appear to be greatly altered, nor are the cell capsules notably thickened. In portions of certain sections nerve bundles are found in a high degree of degeneration; the medullary sheaths have almost entirely disappeared, leaving only granular masses here and there; the axis cylinders are swollen, and the connective tissue and empty nerve sheaths occupy a large portion of the fields. The vessels are somewhat altered.

*
* *

In six of the cases just described the lesions are of an intense degree and unquestionable. In a seventh case (Case VIII) they are much less distinct.

The lesions in the Gasserian ganglion, in the more advanced cases of *tic douloureux*, consist of enormously swollen medullary sheaths and axis cylinders, nerve bundles in which the nerve elements have been destroyed, and only connective tissue is left, atrophied ganglion cells, cells faintly stained, without nuclei or nucleoli, and sclerosed blood vessels in some cases even without a lumen. In all the specimens examined, numerous red blood corpuscles are observed, which doubtless owe their position within the tissues to the surgical interference.

The pathology of *tic douloureux* has not been well known. Some have held that it is a neurosis; others that it is a neuralgia, though this distinction is not very clear; and still others, that it is a neuritis. Some have believed that the disease is a peripheral one, and others that the primary lesion is within the ganglion. There is always a possibility that in some cases the lesion may be a central one.

Putnam says that, as a rule, neuritis is present in trifacial neuralgia, and probably exists far oftener than we think. This seems to me exceedingly probable for the dividing line between neuralgia and neuritis cannot be sharply drawn. One, we are told, is a functional, the other, an organic process; but « functional » is a very comprehensive term. Putnam¹ states that of late years physicians have been more favorable to the view that, in chronic forms of neuralgia at least, the pain is simply the expression of the inflammation of a nerve.

Dana² placed much more value on the condition of the blood vessels than on inflammatory changes in the nerve fibres.

In a recent communication to the writer he expresses the opinion that trifacial neuralgia is due to degenerative neuritis of the peripheral sensory neurones of the fifth nerve, depending on, or associated with, obliterating arteritis.

The investigations by Thoma³ of the blood vessels from the painful areas in supraorbital neuralgia, and his explanation for their sclerotic condition, are most interesting.

Rose⁴ has also remarked on the size of the vessels and the substantial thickness of their walls in some of the cases on which he operated. He found great alteration of the peripheral nerves in trifacial neuralgia. The appearances were those of chronic neuritis, and were often more marked at the peripheral, than at the central end of the nerves.

Microscopical alteration of the peripheral branches of the fifth nerve in cases of tic douloureux have also been noticed by Tuffier⁵, De Schweinitz⁶, Horsley⁷, Tripier⁸, Putnam⁹, Krause¹⁰, etc, and macroscopical changes have been detected by Tuffier¹¹, Mears¹², Tripier¹³, Keen¹⁴, etc.

Krause's¹⁵ book is the most thorough which has as yet appeared on trifacial neuralgia. Though he found alterations in branches of the fifth nerve which had been slowly twisted out, he was unable to detect changes in the vessels. Krause observed marked lesions in the Gasserian ganglion in cases of tic douloureux, but only in one case could he demonstrate changes in the sensory fifth root, and in this case after the pain had disappeared on one side of the face, as a result of excision of the ganglion, it recurred on the other.

Krause could not find the sclerosis of the ganglion, which other writers describe, and which certainly exists in one of Keen's cases (Case IX).

In six of Krause's seven cases, resection of the nerves had preceded, by some years, the excision of the ganglion, and he justly compares his findings with those seen after amputation, but he regards them as too intense to be merely secondary; he thinks the question cannot be positively settled until a ganglion is examined, the peripheral nerves of which have never been resected. This examination has been made in Case VIII of this paper. In none of Krause's

cases did the neuralgia return after excision of the ganglion, even within three and a half years after the operation, and as the peripheral operations did not give permanent relief, and extirpation of the ganglion did do so, he thinks it is allowable to conclude that the cause is to be sought in the Gasserian ganglion.

It seems to me quite possible that the trouble may first be peripheral, and, as resection gives only temporary relief, the recurrence of the pain may be due to extension of the morbid process to the ganglion.

Krause is disposed to regard the changes in the ganglion partly as primary, and partly as secondary from the resection.

The fact that nerve degeneration may extend beyond the spinal ganglia, and affect the posterior roots, must make us prepared for the possibility of an extension of a similar process after extirpation of the Gasserian ganglion.

Other investigators, who have found lesions of the Gasserian ganglion, are Wedl, Rose, Podrazky and Lavéran, Horsley, Putnam, and Antonino D'Antona (all cited by Krause).

The possibility of the changes in the ganglion being secondary, as Krause suggests, is not to be lightly passed over. Lugaro¹⁶ has shown that the nerve cells of the spinal ganglia undergo marked alteration after lesions of the peripheral fibres, and the spinal ganglia are so similar to the Gasserian that the results of these experiments may be applied to the latter.

Fleming has noticed that the cells of the ganglia, on the posterior nerve roots in rabbits and dogs, undergo definite changes as the result of nerve section, or of ligature, and do so at a much earlier period than do the multipolar cells in the cord, beginning, probably, as early as the fourth day, and certainly by the seventh day. The nucleus, and sometimes the nucleolus also, become small, and the nucleus

may be excentric, and even bulge the cell wall. The chromophilic granules are altered, the cells atrophy, and the pericellular lymph spaces become enlarged. Just here, we may mention, however, that Lenhossék's¹⁷ recent studies on fresh spinal ganglia, obtained from an executed man, have taught us that when the ganglia are properly hardened such pericellular lymph spaces do not exist. Fleming¹⁸ also says that large vacuoles are found in some cells. He thinks it is quite comprehensible that the cells of the ganglia should suffer before the cells of the anterior horns, inasmuch as nerve impulses pass normally to them from the site of the lesion.

Kowalewsky¹⁹ cut the sciatic nerve in animals, and injected a few drops of a 5 % chromic acid solution into the central end. The animals were killed two to four days later, and the chromophilic bodies of the cells of the spinal ganglia were found much altered.

If, therefore, such alterations of the ganglion cells occur within a few days after resection of the nerve, we may expect greater changes when the time which has elapsed since the operation is reckoned by years, instead of days. And yet, it is possible that some of the lesions of the ganglion cells, which have been described, are only of a temporary character.

Neuritis may ascend. It seems that the possibility of this, though often disputed, must be acknowledged. M.^{lle} de Majewska²⁰ has recently written a thesis on the subject. She states that the lesions of ascending neuritis are the same as those of ordinary peripheral neuritis; viz. fragmentation of the myelin, multiplication of the nuclei, and alteration of the axis cylinders. There is no reason why this neuritis should not extend to the cells of the Gasserian ganglion.

It would be well, of course, to examine an entire Gasserian ganglion in a case in which resection had never been performed, but the examination of the motor root, in a case

in which the third branch of the fifth had been resected in the portion which contains this root, would also be of value, if done some years after the operation. Should no degeneration of the motor root be found, there would be some evidence that the ascending degeneration had not been important, for this ascending degeneration is not limited to sensory fibres.

Krause could demonstrate changes in the sensory fifth root only in one case. In Case VI, which I have examined, the sensory root is perfectly normal. The cells of the Gasserian ganglion, have each a single axis cylinder, which, at a short distance from the cell body, divides, and one branch passes centrally, and the other peripherally. If, therefore, the lesion is primarily within the ganglion cells, we cannot understand why only the peripheral branches of the axis cylinders are diseased, while the central branches remain normal. The same objection has been raised against the ganglionic theory for the commencement of tabes in the spinal ganglia, only in the latter case the central branches of the axis cylinders are diseased, and the peripheral, as a rule, are intact.

The great and durable improvement, occurring in many cases of trifacial neuralgia after removal of the Gasserian ganglion, would seem to indicate that the cause of the suffering is to be sought, at least in many cases, in the Gasserian ganglion, but it by no means follows that we may expect to find lesions of the ganglion in every case, any more than we may hope to find lesions of the spinal ganglia in every case of tabes in which there has been pain, unless the employment of the method of Nissl changes our views.

We know that a lesion within the cerebrum may produce intense pain as Edinger²¹, Biernacki²², and Kirchhoff²³ have shown, and Gowers²⁴ states that, in a case known to him, irritation of the sensory nucleus of the fifth nerve in

the pons seemed to be the cause of the suffering in the face. Indeed Gowers says distinctly that we know nothing of the sensory function of the posterior ganglia, and are justified in looking to the nerve cells within the cerebrospinal axis as the seat of the morbid process.

In a case of trifacial neuralgia, therefore, attention should be directed, not only to the condition of the Gasserian ganglion, but also, if possible, to that of the sensory nucleus of the fifth nerve, and to the spinal root.

We must acknowledge, it seems to me, that pain is not the usual manifestation of a lesion confined to the brain or cord, and, indeed, the presence of pain in cases of suspected hematomyelia leads one to diagnose hematorrhachis. We do not, as a rule, find pain in chronic degenerative processes of the cord, which respect the posterior roots and meninges, as for instance in syringomyelia, but we find it as an early symptom of tabes, which is also a chronic process, but one which affects the posterior roots.

As Gowers states, vascular dilatation attends functional activity, and it is probably also true that vascular dilatation, if not excessive and too prolonged, causes functional activity. Excessive functional activity of sensory cells may be manifested as pain, but it is possibly equally true that diminution, or imperfect quality of the blood supply, may be a cause of pain. How can we better explain the frequent headache of anemia? If, therefore, we find alteration of the blood vessels within the ganglia, we may, with reasonable suspicion, look upon the condition, in part at least, as the cause of the pain, and may believe that peripheral irritation, which under normal conditions would not be perceived, would be sufficient to produce painful sensations.

As yet, as far as I am able to judge from my researches in the literature, the Gasserian ganglion excised from a case of trifacial neuralgia has never been examined by the

method of Nissl. This method is so important for a study of degenerative changes in nerve cells, that no one can say that such changes are absent until he has used the method. Nissl²⁵ teaches that the employment of the older methods of technique, especially the hardening of the tissue in the chromic salts, and the staining with carmine, are not only unsuitable, but likely to be most misleading.

I am unable, therefore, from a study of these seven cases, and from an examination of the literature, to state whether the lesions of the ganglia are primary or secondary, and if secondary, whether of the nature of ascending neuritis or not. The possibility of the secondary nature of the process within the ganglia in some cases, it seems to me, should not be overlooked. I base the opinion of a possible peripheral involvement, in certain cases, chiefly on the clinical evidence afforded by the permanent relief of pain in some patients by nerve resection, though, unfortunately, such cases are in the minority; and on the examination of Case VIII of this paper, in which the lesions are very slight in comparison with those in the other cases, though the pain had existed for eighteen years. It is true that only a part of the ganglion was obtained in this case, and it is possible that this portion was the least diseased, but it is remarkable that, in all the other cases, intense alteration was found, and in some of these the parts of the ganglia obtained were not larger than in Case VIII. Case VIII is the only one of the seven in which a primary resection of the peripheral branches was not done. The pain involved all three branches of the fifth nerve, and Professor Keen, therefore, attacked the ganglion at once. The possibility of an ascending neuritis in this case, due to nerve resection, is excluded, inasmuch as no operation on the peripheral branches had been performed.

The clinical evidence is of importance, for an absence of pain for two or three years seems to indicate that during

this respite the ganglion cannot be greatly diseased. No branch of the fifth nerve is sharply limited to any one portion of the Gasserian ganglion, and were the ganglion primarily diseased, the resection of one branch would not remove the peripheral irritation transmitted by the other branches to the hypersensitive cells.

There can be no doubt that intense alteration of a chronic, inflammatory character may be found in the Gasserian ganglion in certain cases of *tic douloureux*, and also that the sensory root in such cases may be intact. This, it seems to me, is a satisfactory explanation for the relief of pain experienced by many patients in whom the ganglia have been excised.

The removal of diseased cells within the Gasserian ganglion, which are capable of responding abnormally to every peripheral irritation, may well be attended with the relief of pain. Excision of the ganglion destroys at once the paths of painful sensation from a large area.

The integrity of the sensory root, in the case in which the whole ganglion was removed by Professor Keen, is a fact of considerable importance. It teaches that, though the ganglion may be greatly diseased, the process may be arrested at this point. In the other case in which the sensory root was examined, the only other case (Krause) in which it is positively stated that such an examination was made (though Krause may have examined the sensory root in some of his other cases) the fibres were found diseased, and the process extended to the other side of the face. This report, and the four cases (one reported by Rose, two by Keen, and one by Dana) in which the pain returned after removal of the ganglion, though we are not sure that all portions of the ganglion were excised in these cases, must make us prepared for the possibility of a renewal of the suffering in some instances, even after the excision of the Gasserian ganglion.

I am more than ever inclined to believe, from a study of these cases, that neuralgia cannot be sharply separated from neuritis, and in some cases of so-called chronic neuralgia, such as obstinate sciatica, I believe we may be able by the microscope to detect evidences of chronic inflammation.

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EXPLICATION OF THE PLATES.

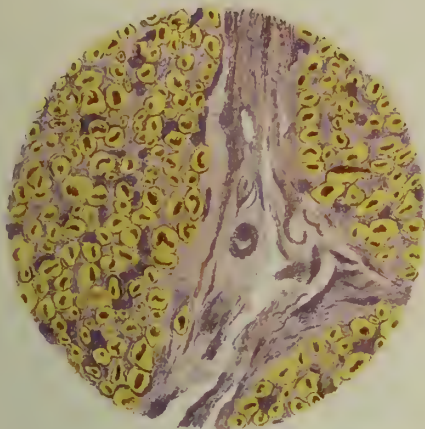
PLATE I.

- FIGURE *a* — Portion of the sensory root from Case VI. The nerve fibres are normal.
- FIGURE *b* — Portion of the second branch of the trigeminal nerve, near the Gasserian ganglion, from Case VI. The axis cylinders have entirely disappeared, and the medullary sheaths are enormously swollen. In many places the medullary substance of two or more nerve fibres has united into irregularly-shaped masses.
- FIGURE *c* — One of the nerve bundles within the Gasserian ganglion, from Case VI. Numerous swollen and irregularly-formed axis cylinders may be seen. In most portions of the field these appear as drops of a red, hyaline-like substance, but in one portion an axis cylinder of considerable length may still be seen.
- FIGURE *d* — Portion of the Gasserian ganglion at the entrance of the third branch of the trifacial nerve, from Case VI. The medullary sheaths are most irregularly swollen, and at the right of the field empty nerve sheaths are observed (Method of Azoulay).
- FIGURE *e* — Swollen medullary sheaths, and empty nerve sheaths, from the Gasserian ganglion, in Case VII.

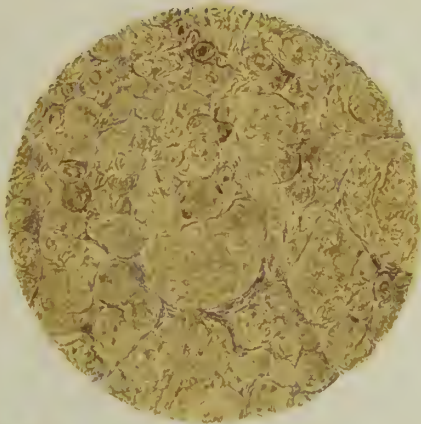
PLATE II.

- FIGURE *f* — Part of the Gasserian ganglion, from Case IX. Only two ganglion cells are seen in the drawing: the others have degenerated, and their places are occupied by connective tissue. This portion of the ganglion presents a high degree of sclerosis.
- FIGURE *g* — Portion of a normal Gasserian ganglion. A sharp contrast is offered to the preceding section.
- FIGURE *h* — Blood vessels from the Gasserian ganglion, in Case IX. The walls are greatly thickened, and the lumen of the large vessel has been almost entirely obliterated. In one place the innermost layers of the vessel have contracted from the outer during the process of hardening. Smaller vessels, in the upper part of the field, are entirely closed.
- FIGURE *i* — A nerve bundle of the trigeminus close to the Gasserian ganglion, from Case X. Only a few nerve fibres are present, and everywhere an abundance of connective tissue is seen. Three much swollen medullary sheaths are in the field.

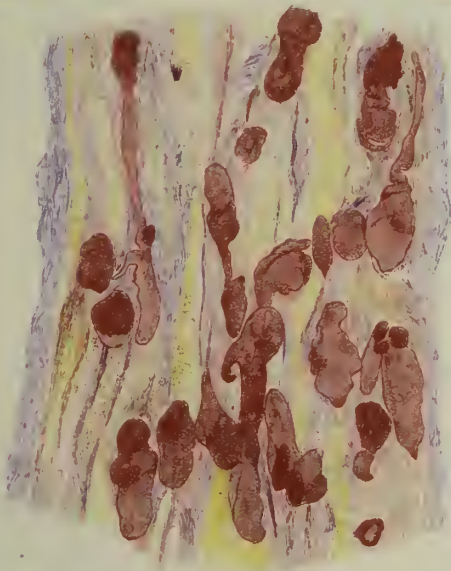




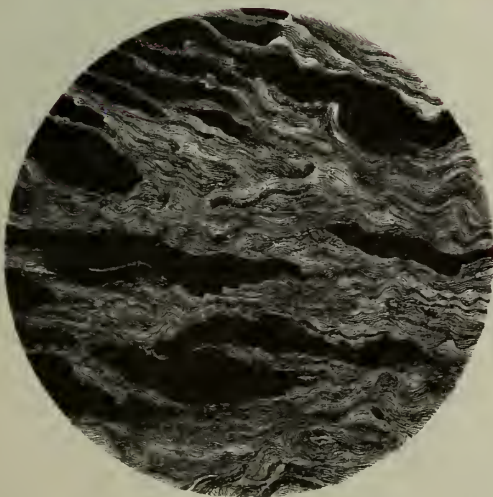
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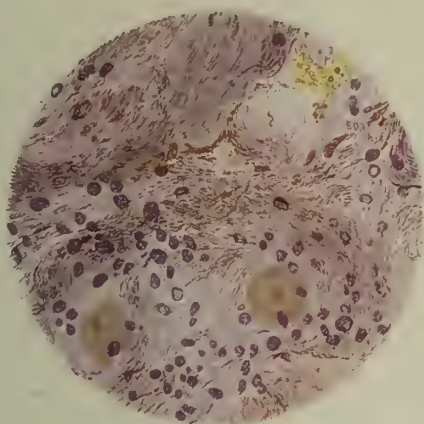
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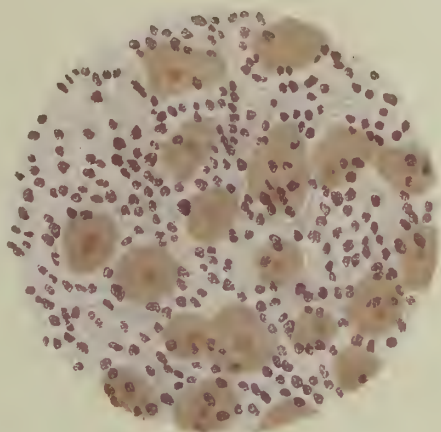
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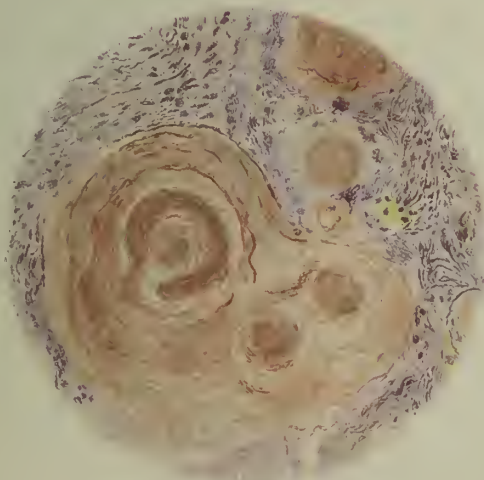
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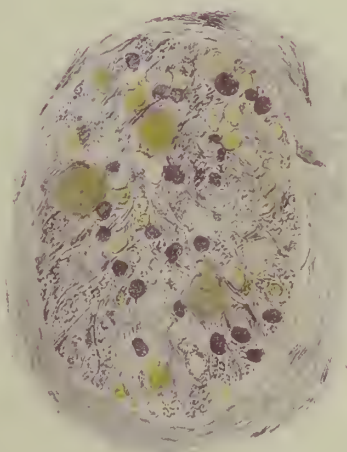
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